

Claims 1-12, 36-54, 60-78, 83-86 and 93-117 are withdrawn from further consideration, as being drawn to a non-elected invention.

Claims 13-35, 55-59, and 79-81 are pending

Claims 82 and 87-92 are allowed.

35 U.S.C. § 102(a) and (e) Rejections

Claims 13-18, 20-35, 55-59 and 79 are rejected under 35 U.S.C. § 102(a) and (e) as being anticipated by Heller et al. (U.S. Patent No. 5,632,957). The Examiner asserts that the abstract and Figures 1 and 6 of Heller et al., taken as a whole discloses a PCR/diagnostic system that anticipates the cited claims. More particularly, Heller et al. allegedly discloses a system for heating and cooling PCR reaction with detection of the product wherein the system is implemented on a microchip where the sample wells are smaller than 1 ml. The Applicants respectfully submit that Heller et al. do not anticipate the claimed invention.

Heller et al. describe an analytical system of sample preparation, hybridization and detection. It includes data analysis which integrates multiple steps within a combined system. Within the system described, charged materials, such as DNA, are transported via free field electrophoresis and bind to a support. DNA complexity is reduced by restriction enzyme digestion, followed by transport of the cleaved DNA to an analytical chip (APEX), as schematically depicted in Figures 1 and 6. A controller activates the underlying electrodes in an APEX device by the application of a controlled potential to the electrode or by the sourcing of a controlled current through the electrode. Electronic stringency control is used to retain DNA at an attachment layer and to control the efficacy of e.g., hybridization. By raising the electric potential at the electrodes to create a field sufficient to remove partially hybridized DNA

sequences, containing hybridization complexes of single mismatches, such as point mutations, may be identified.

The present invention teaches a device for performing PCR and monitoring the reaction in real time during temperature cycling. The device comprises a sample chamber whose temperature is rapidly and accurately modulated over a range of temperature needed to carry out a number of biological procedures, such as PCR. A programmable controller regulates the temperature of the sample inside the sample chamber. In particular, the invention of claims 13-18 and claims 20-32 comprises (i) a sample container; (ii) means for heating the PCR sample; (iii) means for cooling the PCR sample; and (iv) a controller repeatedly operating the means for heating and cooling to subject the PCR sample to thermal cycling. The invention of claims 33-35 comprises (i) a plurality of sample containers; and (ii) means for forcing hot fluid and cool fluid into contact with the plurality of sample containers. The invention of claims 55-59 comprises a thermal cycling means for repeatedly heating and cooling a first and a second holding means in both a non-monitoring and monitoring position to carry out thermal cycling on both a first and a second biological sample. The claimed invention of claim 79 comprises a sample vessel holder which comprises an optically transparent material.

The system described by Heller et al. does not anticipate the invention as set forth in claims 13-18, 20-35, 55-59, and 79.

As the Examiner is aware, the law is well established that in order to anticipate a claim, the prior art must disclose "each and every element" of the claimed invention. *SSIH Equipment S.A. v. U.S. Inc. Int'l Trade Commission*, 218 USPQ 678, 688 (Fed. Cir. 1983). As stated by the Federal Circuit in *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990), "[f]or a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention

must be identically shown in a single reference." (*emphasis added*). See also *Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc.*, 33 USPQ2d 1496 (Fed. Cir. 1995).

There are several striking differences between the system described by Heller et al. and the present invention.

First, Heller et al. describe a system wherein a charged sample, such as DNA, is transported via free field electrophoresis to bind to a support and by the same means is translated to various microlocations for further manipulations. The claimed invention clearly requires the sample, such as DNA, to be confined to a sample container and no transport of the sample to various microlocations for further manipulations is required. Heller et al. do not describe (i) a sample container or (ii) a plurality of sample containers or (iii) a sample vessel holder which comprises an optically transparent material. These elements are in each of the independent claims 13, 33, and 79, respectively.

Second, Heller et al. describe a system wherein denaturation and hybridization is controlled electronically, *i.e.*, by charging the electric potential at the electrodes to create an electric field which facilitates hybridization of DNA sequences or the removal of partially hybridized DNA sequences. In the claimed invention, hybridization of DNA (oligonucleotides) to a DNA target is achieved by a controller which allows for the repeatedly operating of a heating and cooling means. Heller et al. do not describe (i) means for heating the PCR sample; (ii) means for cooling the PCR sample, (iii) a controller repeatedly operating the means for heating and cooling to subject the PCR sample to thermal cycling, (iv) a plurality of sample containers, and (v) means for forcing hot fluid and cool fluid into contact with the plurality of sample containers. These are elements of independent claims 13 and 33, respectively. In addition, a limitation of the independent claim 59, requires (vi) a thermal cycling means for repeatedly heating and cooling a first and a second holding means in both a non-monitoring and monitoring position to carry out

thermal cycling on both a first and a second biological sample. This aspect of the invention is not disclosed by Heller et al.

In summary, the system described by Heller et al. do not anticipate the invention claimed in independent claims 13, 33, 55 and 79. As such, Heller et al. cannot anticipate the dependent claims thereof because Heller et al. does not disclose "each and every element" of the claimed invention.

The Applicants submit that the claims are now in condition for allowance and an early notification of such is respectfully solicited.

In after review of Applicants' response, the Examiner has further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (317) 231-7258.

The Commissioner is authorized to charge any additional fees, including any extension fees, which may be required, or credit any overpayment to Deposit Account No. 10-0435 with reference to our matter 7475-29601.

Respectfully submitted,



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